DETAILED ACTION

The amendment filed March 22, 2010 have been received and entered into the application.

Response to Arguments

Applicant's arguments filed March 22, 2010 have been fully considered but they are not persuasive. Applicant first argues that the pending claims relate to a very specific patient population suffering from chronic mechanical back pain which is not disclosed or suggested by Fox. Applicant further argues that the hyperalgesia test models disclosed by Fox cannot be applied to chronic mechanical pain because the pain associated with hyperalgesia is an acute response to a painful stimulus. This is not persuasive because the instant invention of the treatment of "chronic mechanical back pain" as defined in the specification (page 7 third full paragraph) has been carefully reviewed and considered. It is noted that the term “chronic mechanical back pain" is defined as any back pain lasting more than twelve weeks which is not caused by cancer, or an osteoporotic compression fracture. Therefore, the term chronic mechanical back pain includes any back pain that is chronic which is not caused by cancer, or an osteoporotic compression fracture.

Applicant's attention is drawn to the cited Fox reference which demonstrates that **Zoledronate reverses mechanical hyperalgesia** in model of **chronic inflammatory** and **neuropathic pain** in the rat (see column 6 [0106]). Moreover, in a model of chronic neuropathic pain induced by unilateral partial sciatic nerve ligation, zoledronate produced a 40% reversal of mechanical hyperalgesia with a significant reduction of contralateral paw withdrawal thresholds at the highest dose. None of the subjects demonstrated by the examples above indicate that the subject with chronic neuropathic pain or mechanical hyperalgesia was suffering from cancer or osteoporotic compression fracture. Therefore, the subject population demonstrated by Fox encompasses and obviates Applicant's definition of chronic pain not caused by cancer, or an osteoporotic compression fracture. Applicant argues that those of ordinary skill in the art would not readily appreciated that method for treating acute forms of pain are not necessarily applicable to treating pain because it is well established that "chronic pain" relates to pain that is "prolonged" or "long-term" while "acute pain" is defined as "brief" or "not chronic pain". This is not persuasive because the regardless of how "chronic pain" and "acute pain" are interpreted differently, it does not change the most relevant and demonstrated example of Fox comprising the data showing that zoledronate reverses mechanical hyperalgesia in models of chronic inflammatory pain in rats. Therefore, there is a reasonable expectation of successfully treating any pain not caused by cancer or osteoporotic compression fracture including pain in the back not caused by cancer or compression fracture because zoledronate reverses mechanical hyperalgesia in models of chronic inflammatory pain as demonstrated by Fox. Applicant argues that Fox

provides no teaching which would have led the skilled artisan to administer bisphosphonates for prolonged pain relief of at least three month since Fox suggests that bisphosphonates only exhibit a short term effect. This is not persuasive because Fox et al. teach the effective dosage range of bisphosphonates of 0.01-10.0mg/kg which encompasses Applicants' range set forth in the claim 7. Moreover, Fox et al. teach that the doses of bisphosphonates including zoledronic acid and pamidronate for the treatment of pain can be administered once daily, once weekly, **once every month, once every three month, once every six months or once a year**. (abstract, claims [0075]-[0077]). Accordingly, Fox teach that bisphosphonates such as pamidronate and zoledronic acid are effective for the treatment of pain with the same effective amounts with the same dosing frequency as instantly claimed, therefore, the duration of analgesic action of bisphosphonates would be obviously retained and last until the next dosing time, e.g. every three month or every once every six month or once a year taught by Fox. Therefore, it would have been obvious to one of ordinary skill in the art to employ bisphosphonates e.g. pamidronate or zoledronate for the treatment of any mechanical or an inflammatory pain regardless of the cause because the effectiveness of pamidronate or zoledronate in pain management is well known in the art in view of Fox et al and Geusens et al. Applicant argues that the Examiner's reliance on Geusens for disclosing the use of bisphosphonates for treating back pain is a mischaracterization of the reference because Geusens does not teach that bisphosphonate has any direct effect on pain relief. This is not persuasive because Geusens reference was cited just to show that extreme back pain in general as the result of multiple vertebral fractures

has been treated with pamidronate in an adolescent boy. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Allowable Subject Matter

Claims 9 drawn to specific subject population of human would be favorably considered since Fox in their illustrated example ([0105]) teach that pamidronate was weakly active in the model of neuropathic pain producing a maximal 20% reversal of hyperalgesia in a rat.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-7 and 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fox et al. (US 2004/0063670A1) in view of Geusens et al. (2001) of record.

Fox et al exemplify both pamidronate and zoledronate for the treatment of inflammatory hyperalgesia and mechanical hyperalgesia. (see abstract, examples, claims). Fox et al. teach that the doses of bisphosphonates including zoledronic acid and pamidronate for the treatment of pain can be administered once daily, once weekly, **once every month, once every three month, once every six months or once a**

year. (abstract, claims [0075]-[0077]). Fox et al teach a method for the treatment of pain, in particular antinociceptive or anti-allodynic treatment of pain, in a patient in need of such treatment, e.g. a patient with osteoporosis or osteopenia, a tumor patient or a patient suffering from an inflammatory disease, which comprises administering an effective amount of a bisphosphonate, e.g. zoledronic acid or salt or hydrates thereof, to the patient. Fox et al teach that the effective dosages of zoledronate and pamidronate are from 0.002-20.0mg/kg, especially 0.01-10.0mg/kg. If desired, this dose may be also taken in several optionally equal or partial doses. Fox et al teach that the dose mentioned above, can be either administered as a single dose (which is preferred) or in several partial doses. Fox et al teach that the bisphosphonates can be administered parenterally, preferably intravenously. ([0083]).

Fox et al. do not expressly teach the duration of pain relief for at least three month following the most recent administration of pamidronate and zoledronic acid; the specific chronic spinal mechanical pain as being any back pain lasting more than twelve weeks which is not caused by cancer, or an osteoporotic compression fracture as defined in the specification page 7; and the treatment comprising providing prolonged pain relief.

Geusens et al. teach that an 18-year-old boy presented with extreme back pain as the result of multiple vertebral fractures was treated with intermittent intravenous bisphosphonate such as **pamidronate**. (abstract). Geusens et al. teach that intermittent IV infusions of pamidronate were given at dose of 30mg infusion, 300 mg in total over 9 month. (page 390 right-hand column first sentence originated from left-hand

column, bottom). The boy progressively recovered from **back pain** and is now, at age 20, fully ambulant. (abstract).

It would have been obvious to one of ordinary skill in the art to employ pamidronate or zoledronate for the treatment of any mechanical or an inflammatory pain regardless of the cause because the effectiveness of pamidronate or zoledronate in pain management is well known in the art in view of Fox et al and Geusens et al. One would have been motivated to employ bisphosphonates including pamidronate and zoledronate for the treatment of pain at any cause in order to achieve their beneficial analgesic effect in the patient disclosed by both Fox et al. and Geusens et al. There is a reasonable expectation of successfully treating any pain particularly back pain regardless of a cause because bisphosphonates including pamidronate and zoledronate having analgesic effect are well disclosed by the cited references. With regard to the duration of pain relief for at least three months following the most recent administration and prolonged pain relief such is obvious because Fox teach that bisphosphonates such as pamidronate and zoledronic acid are effective for the treatment of pain with the same effective amounts as instantly claimed and can be administered every 3 month to a year. Therefore, such analgesic effect for the treatment of pain would be obviously retained in the patients who needs the dosages every three month or every once every six month or once a year with the administration of the same effective amounts taught by Fox et al.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Communication

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER M. KIM whose telephone number is (571)272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on 571-272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JENNIFER M KIM/
Primary Examiner, Art Unit 1628

Jmk
June 14, 2010